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## CLINICAL RESEARCH

# Renal function and outcomes after catheter ablation of patients with atrial fibrillation: The Guangzhou atrial fibrillation ablation registry



*Fonction rénale et évènement au décours d'une ablation par cathéter de fibrillation atriale : The Guangzhou atrial fibrillation ablation registry*

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**Abbreviations:** AF, atrial fibrillation; BNPB, -type natriuretic peptide; CA, catheter ablation; CI, confidence interval; CKD, chronic kidney disease; CRP, C-reactive protein; HR, hazard ratio; ICD, International classification of diseases.

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**KEYWORDS**

Atrial fibrillation;  
Catheter ablation;  
Recurrence;  
Chronic kidney  
disease

**Summary**

*Introduction.* — Chronic kidney disease (CKD) has been associated with incident atrial fibrillation (AF) and its complications, but data from Asian cohorts are limited.

*Aim.* — To explore the relationship of AF recurrence after catheter ablation (CA) with eGFR as a continuous variable, and with different renal function categories (normal: estimated glomerular filtration rate [eGFR]  $\geq 90$  mL/min/1.73 m<sup>2</sup>; mild CKD: eGFR 60–89 mL/min/1.73 m<sup>2</sup>; moderate CKD: eGFR 45–59 mL/min/1.73 m<sup>2</sup>; severe CKD:  $<45$  mL/min/1.73 m<sup>2</sup>), using data from the Guangzhou Atrial Fibrillation Ablation Registry.

*Methods.* — We studied consecutive symptomatic adult patients with non-valvular AF, refractory to at least one antiarrhythmic drug and eligible for CA, in Guangdong General Hospital between June 2011 and August 2015.

*Results.* — Data were available from 1407 consecutive patients (mean age  $57.3 \pm 11.5$  years; 68% men) with non-valvular AF undergoing radiofrequency or cryoballoon ablation. During a mean follow-up of  $20.7 \pm 8.8$  months, 18.6% of patients with paroxysmal AF and 50.5% with non-paroxysmal AF had AF recurrence. On multivariable analysis, eGFR (hazard ratio [HR] 0.97, 95% confidence interval [CI] 0.96–0.97) was an independent risk factor for AF recurrence, with a good predictive value (area under the curve 0.74, 95% CI 0.72–0.77;  $P < 0.01$ ). In the normal renal function, and mild, moderate and severe CKD categories, AF recurrence rates were 11.5%, 29.3%, 72.0% and 93.3%, respectively. Compared with normal renal function, there were stepwise increased risks of AF recurrence with mild CKD (HR 3.30, 95% CI 2.55–4.26;  $P < 0.01$ ), moderate CKD (HR 9.43, 95% CI 6.76–13.16;  $P < 0.01$ ) and severe CKD (HR 12.35, 95% CI 6.93–21.99;  $P < 0.01$ ).

*Conclusions.* — In a large cohort of Asian patients with AF, renal dysfunction increased the risk of AF recurrence after CA. AF recurrence gradually increased with worsening kidney function in this cohort.

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**MOTS CLÉS**

Fibrillation atriale ;  
Ablation de  
cathéter ;  
Récurrence de  
fibrillation atriale ;  
Insuffisance rénale  
chronique

**Résumé**

*Introduction.* — L'insuffisance rénale chronique (IRC) est associée à la fibrillation atriale (FA) incidente et à ses complications, mais les données émanant du continent asiatique sont en nombre limité.

*Objectif.* — Évaluer la relation entre la récurrence de fibrillation atriale au décours d'une ablation par cathéter en prenant en considération le taux de filtration glomérulaire comme une variable continue, et donc le type d'altération de la fonction rénale (normale : taux de filtration glomérulaire estimé  $\geq 90$  mL/mn/1,73m<sup>2</sup> ; insuffisance rénale chronique modérée : TFG : 60–89 mL/mn/1,73m<sup>2</sup> ; insuffisance rénale chronique moyenne : TFG 45–59 mL/mn/1,73 m<sup>2</sup> et insuffisance rénale chronique sévère : TFG  $< 45$  mL/mn/1,73m<sup>2</sup>) en prenant en considération les données du registre Guangzhou atrial fibrillation ablation registry.

*Méthode.* — Nous avons étudié des patients adultes symptomatiques ayant une FA non valvulaire, réfractaire à au moins un médicament anti-arythmique et éligibles pour une ablation par cathéter entre juin 2011 et août 2015.

*Résultats.* — Les données sont disponibles chez les 1407 patients consécutifs (âge moyen  $57,3 \pm 11,5$  ans ; 68 % d'hommes) ayant une FA non valvulaire et une indication à une ablation par radiofréquence ou par cryo-ablation pour fibrillation atriale. Pendant un suivi moyen de  $20,7 \pm 8,8$  mois, 18,6 % des patients en FA paroxystique et 50,5 % en FA non paroxystique ont présenté une récurrence de FA. L'analyse multivariée montre que le TFG (HR 0,97 ; IC 95 % 0,96–0,97) constitue un facteur de risque indépendant de récurrence de la FA avec une bonne valeur prédictive positive (surface sous la courbe ROC 0,74, IC 95 % 0,72–0,77,  $p < 0,01$ ). Le taux de récurrence de la FA est de 11,5 %, 29,3 %, 72,0 % et 93,3 % respectivement. Comparés au groupe de patients ayant une fonction rénale normale, il est noté une augmentation du risque de récurrence dans l'insuffisance rénale chronique modérée (HR 3,3, IC 95 % 2,55–4,26 ;  $p < 0,01$ ), l'insuffisance rénale moyenne (HR 9,43, IC 95 % 6,76–13,13,  $p < 0,01$ ) et dans l'insuffisance rénale chronique sévère (HR 12,35, IC 95 % 6,93–21,99,  $p < 0,01$ ).

*Conclusion.* – Dans une cohorte de patients originaire du continent asiatique en FA non valvulaire, la dysfonction rénale augmente le risque de récurrence de la FA au décours d'une ablation par cathéter. Le taux de récurrence augmente de façon progressive au prorata de l'altération de la fonction rénale dans cette cohorte.

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## Background

Catheter ablation (CA) has been recommended as a first-line treatment option for refractory symptomatic atrial fibrillation (AF) [1]. Despite advances in techniques, AF recurrence after CA is still an important problem, especially in long-term follow-up [2].

AF is present in 15–20% patients with chronic kidney disease (CKD), which has a close bidirectional relationship with cardiovascular disease, including AF [3–5]. CKD has been associated with incident AF and its complications as well as with arrhythmia recurrence after CA, but much of the data were from Western cohorts. Relatively limited data are available on the impact of renal (dys)function on arrhythmia outcome after CA in Asian patients [6,7]. There are also limited data on the relationship between arrhythmia outcome and different categories of renal function.

In this report from the Guangzhou AF Ablation Registry, we explored the relationship of AF recurrence after CA with estimated glomerular filtration rate (eGFR) as a continuous variable, and with different categories of renal function.

## Methods

We studied 1407 consecutive symptomatic adult patients with non-valvular AF who were refractory to at least one antiarrhythmic drug and eligible for CA in Guangdong General Hospital between June 2011 to August 2015. Baseline clinical data were acquired from patients' medical records in the hospital's patient database. All patients provided written informed consent. The study protocol was approved by the Clinical Research Ethics Committee of Guangdong General Hospital.

Paroxysmal AF was defined as AF that terminated spontaneously or with intervention within 7 days, persistent AF was defined as AF that lasted  $\geq 7$  days and long-standing persistent AF was defined as AF that lasted  $> 1$  year [8]. The term "non-paroxysmal AF" included persistent AF and long-standing persistent AF. All patients had at least one symptomatic AF episode recorded before the ablation procedure. Recurrence was defined as any symptomatic or asymptomatic atrial tachyarrhythmia (AF, atrial tachycardia and/or atrial flutter) lasting  $> 30$  seconds. A recurrence recorded within the 3-month "blinking period" after the ablation was defined as early recurrence.

The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula ( $186 \times$  serum

creatinine $^{-1.154} \times$  age $^{-0.203} \times [1.210$  if Black]  $\times [0.742$  if female]) [9]. The relationship of AF recurrence after CA was evaluated in relation to eGFR as a continuous variable, and to categories of renal function, as follows: normal (eGFR  $\geq 90$  mL/min/1.73 m $^2$ ); mild CKD (eGFR 60–89 mL/min/1.73 m $^2$ ); moderate CKD (eGFR 45–59 mL/min/1.73 m $^2$ ); and severe CKD (eGFR  $< 45$  mL/min/1.73 m $^2$ ) [3,10].

## Ablation procedure

All patients received anticoagulation therapy before, during and after the procedure, following guideline recommendations [1]. Left atrial thrombosis was excluded by transoesophageal echocardiography or left atrial computed tomography, and antiarrhythmic drugs were discontinued before the procedure. Procedures were performed under modest sedation with fentanyl. Activated clotting time was maintained between 250 and 350 seconds by heparin doses. Circumferential pulmonary vein isolation was performed under the guidance of a three-dimensional mapping system (Carto $^{\circledR}$  2 or 3, Biosense Webster Inc., Irvine, CA, USA; or EnSite $^{\text{TM}}$  NavX $^{\text{TM}}$  Classic and EnSite $^{\text{TM}}$  NavX $^{\text{TM}}$  Velocity $^{\text{TM}}$ , St. Jude Medical, St. Paul, MN, USA) in patients undergoing radiofrequency ablation. Alternatively, a cryoballoon catheter (Cryoconsole Cardiac Cryoablation System, Medtronic Inc., Minneapolis, MN, USA) was used to perform cryoballoon ablation [11]. Bidirectional conduction block from the atrium to the pulmonary veins and vice versa was judged as the ablation endpoint.

Cavotricuspid isthmus bidirectional block and other additional ablations, such as superior vena cava isolation, linear ablation of the left atrial roof or mitral isthmus and complex fractionated atrial electrograms, were performed selectively to ensure sinus rhythm restoration. Pharmacological cardioversion (ibutilide or amiodarone) or electrical cardioversion was used to restore sinus rhythm where necessary.

## Follow-up

Follow-up visits included a physical examination, 12-lead electrocardiogram and 24-hour Holter electrocardiogram, and were scheduled at discharge, at 1, 3 and 6 months, and every 6 months thereafter. Additional electrocardiogram or 24-hour Holter monitors were performed in patients who complained of symptoms suggestive of arrhythmia recurrence. In all patients, oral anticoagulants and amiodarone

(or propafenone) were given within the blanking period. Afterwards, oral anticoagulants were continued in patients with a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of  $\geq 2$ . Arrhythmia recurrence was defined as the study endpoint. Once arrhythmia recurrence was confirmed, observation of the patient ended. Patients without evidence of recurrence were followed for a minimum of 12 months.

## Statistical analysis

All continuous variables are presented as means  $\pm$  standard deviations, and categorical variables are summarized as percentages. An analysis of variance least significant difference test or the  $\chi^2$  test was used to test the difference between

continuous or categorical variables among the four renal function categories. The association of the clinical variables with AF recurrence was analysed using univariate and covariate Cox regression models.

Cox proportional-hazards models with time-dependent covariates for changing eGFR and AF recurrence were built to evaluate the independent effects of different degrees of eGFR on outcomes. The area under the receiver operating characteristic curve was calculated to test the predictive probability of eGFR for AF recurrence, and a cut-off analysis was performed to calculate specificity and sensitivity. A survival analysis was used to test the differences in time-dependent outcomes in patients between cut-off values or four categories of eGFR. A two-sided *P* value

**Table 1** Clinical characteristics in relation to categories of renal function.

Characteristics	Total (n = 1407; 100%)	Normal renal function <sup>a</sup> (n = 566; 40.2%)	Mild CKD <sup>a</sup> (n = 726; 51.6%)	Moderate CKD <sup>a</sup> (n = 100; 7.1%)	Severe CKD <sup>a</sup> (n = 15; 1.1%)	<i>P</i>
Age (years)	57.3 $\pm$ 11.5	53.7 $\pm$ 12.6	58.8 $\pm$ 9.9	65 $\pm$ 8.6	65.7 $\pm$ 11.2	< 0.01
LAD (mm)	36.9 $\pm$ 5.3	36 $\pm$ 5.3	37.4 $\pm$ 5.2	37.9 $\pm$ 5.6	39.2 $\pm$ 4.9	< 0.01
BMI (kg/m <sup>2</sup> )	24.5 $\pm$ 3.3	24.2 $\pm$ 3.2	24.8 $\pm$ 3.2	24.8 $\pm$ 4.1	23.9 $\pm$ 3.0	0.023
BNP (pg/mL)	319 $\pm$ 465	199 $\pm$ 289	347 $\pm$ 493	726 $\pm$ 695	859 $\pm$ 474	< 0.01
CRP (mg/dL)	2.3 $\pm$ 3.8	1.8 $\pm$ 4.1	2.4 $\pm$ 3.2	4.0 $\pm$ 4.5	4.9 $\pm$ 2.8	< 0.01
Ejection fraction (%)	64.7 $\pm$ 6.1	65.1 $\pm$ 6.2	64.6 $\pm$ 6.0	63.3 $\pm$ 6.5	63.9 $\pm$ 6.5	0.03
Follow-up period (months)	20.7 $\pm$ 8.8	22.8 $\pm$ 7.3	20.1 $\pm$ 9.1	13.9 $\pm$ 9.3	12.7 $\pm$ 7.5	< 0.01
Female	449 (31.9)	188 (33.2)	196 (27.0)	45 (45.0)	5 (66.7)	< 0.01
Non-paroxysmal AF	320 (22.7)	102 (18.0)	184 (25.3)	45 (45.0)	5 (33.3)	< 0.01
COPD	9 (0.6)	0	6 (0.1)	3 (3.0)	0	< 0.01
Alcohol consumption	75 (5.3)	28 (4.9)	41 (5.6)	4 (4.0)	2 (13.3)	0.47
Smoking	244 (17.3)	96 (17.0)	134 (18.5)	12 (12.0)	2 (13.3)	0.42
History of CHF	71 (5.0)	17 (3.0)	40 (5.5)	12 (12.0)	2 (13.3)	< 0.01
Hypertension	508 (36.1)	149 (26.3)	295 (40.6)	55 (55.0)	9 (60.0)	< 0.01
Diabetes mellitus	143 (10.2)	46 (8.1)	79 (10.9)	15 (15.0)	3 (20.0)	0.07
Stroke	84 (6.0)	27 (4.8)	42 (5.8)	12 (12.0)	3 (20.0)	< 0.01
CAD	105 (7.5)	29 (5.1)	58 (8.0)	14 (14.0)	4 (26.7)	< 0.01
Cryoablation	74 (5.3)	28 (4.9)	35 (4.8)	10 (10.0)	1 (6.7)	0.18
Electrical cardioversion	157 (11.2)	52 (9.2)	90 (12.4)	12 (12.0)	3 (20.0)	0.20
Early recurrence	317 (22.5)	83 (14.7)	181 (24.9)	41 (41.0)	12 (80.0)	< 0.01
Recurrence	364 (25.9)	65 (11.5)	213 (29.3)	72 (72.0)	14 (93.3)	< 0.01
ST ablation catheter	247 (17.6)	99 (17.5)	131 (18.0)	16 (16.0)	1 (6.7)	0.68
PV isolation	1391 (98.9)	557 (98.4)	719 (99.0)	100 (100)	15 (100)	0.56
CFAE ablation	35 (2.9)	11 (1.9)	17 (2.3)	6 (6.0)	1 (6.7)	0.08
CTI ablation	337 (24.0)	121 (21.4)	190 (26.2)	22 (22.0)	4 (13.3)	0.24
SVC ablation	87 (6.2)	40 (7.1)	40 (5.5)	6 (6.0)	1 (6.7)	0.72
Antiarrhythmic drugs failed	1179 (83.8)	480 (84.8)	607 (83.6)	81 (81.0)	11 (73.3)	0.12
Pharmacological cardioversion	221 (15.7)	81 (14.3)	116 (16.0)	21 (21.0)	3 (20.0)	0.36
Vascular disease	49 (3.5)	13 (2.3)	27 (3.7)	9 (9.0)	0 (0)	< 0.01

Data are expressed as mean  $\pm$  standard deviation or number (%).  $\chi^2$  and analysis of variance least significant difference tests. AF: atrial fibrillation; BMI: body mass index; BNP: B-type natriuretic peptide; CAD: coronary artery disease; CFAE: complex fractionated atrial electrogram; CHF: congestive heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; CTI: cavotricuspid isthmus; eGFR: estimated glomerular filtration rate; LAD: left atrial diameter; PV: pulmonary vein; ST: SMARTTOUCH<sup>®</sup> (Biosense Webster Inc., Irvine, CA, USA); SVC: superior vena cava.

<sup>a</sup> Categories of renal function [3]: normal, eGFR  $\geq 90$  mL/min/1.73 m<sup>2</sup>; mild CKD, 60–89 mL/min/1.73 m<sup>2</sup>; moderate CKD, 45–59 mL/min/1.73 m<sup>2</sup>; severe CKD, < 45 mL/min/1.73 m<sup>2</sup>.

**Table 2** Multivariable Cox regression analysis<sup>a</sup> of risk factors for atrial fibrillation recurrence after catheter ablation.

Risk factor	HR (95% CI)	P
Age	0.97 (0.96–0.98)	< 0.01
AF types	1.78 (1.42–2.23)	< 0.01
Early recurrence	3.77 (3.02–4.72)	< 0.01
History of CHF	1.33 (1.13–1.57)	< 0.01
LAD (mm)	1.07 (1.04–1.09)	< 0.01
eGFR (mL/min/1.73 m <sup>2</sup> )	0.97 (0.96–0.97)	< 0.01
BMI (kg/m <sup>2</sup> )	1.06 (1.02–1.10)	< 0.01

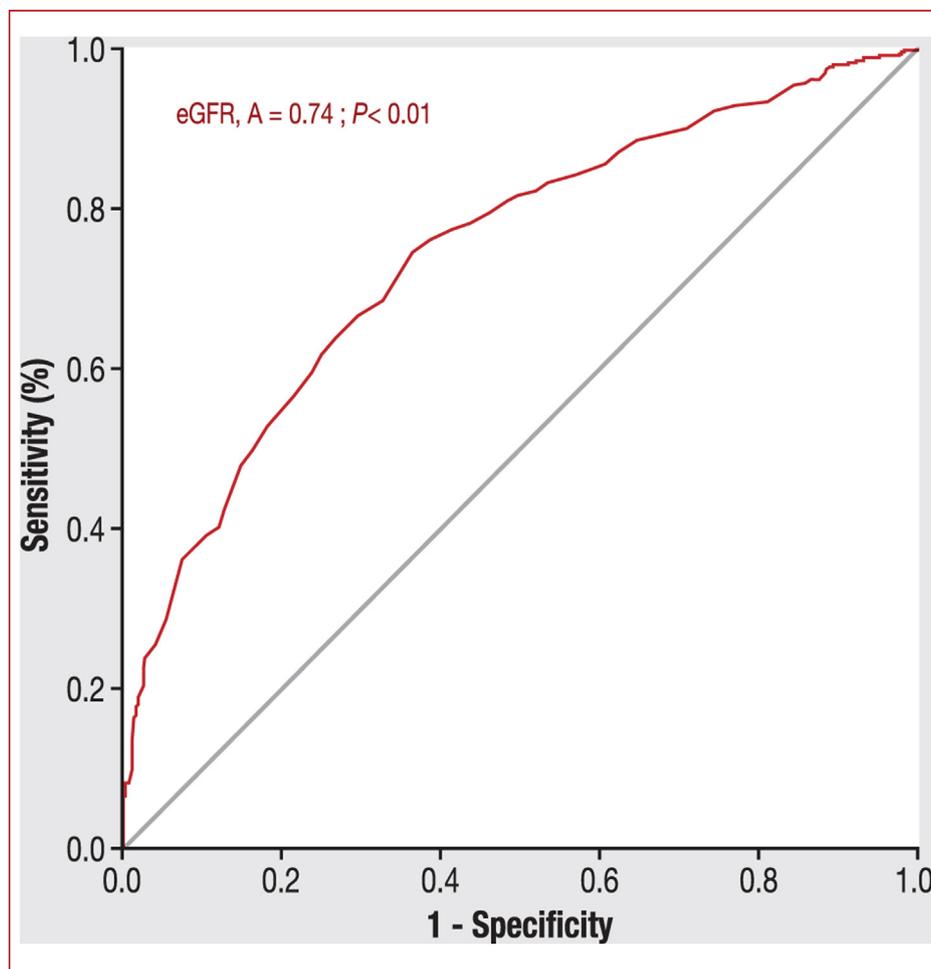
AF: atrial fibrillation; BMI: body mass index; CHF: congestive heart failure; CI: confidence interval; eGFR: estimated glomerular filtration rate; HR: hazard ratio; LAD: left atrial diameter.

<sup>a</sup> Adjusted for sex, bundle branch block, AF duration, chronic obstructive pulmonary disease, alcohol consumption, smoking, hypertension, diabetes mellitus, stroke/transient ischaemic attack, coronary artery disease, ejection fraction and vascular disease.

of < 0.05 was considered statistically significant. Analyses were performed using the SPSS software, version 20.0 (IBM Corporation, Armonk, NY, USA).

## Results

Baseline characteristics for the normal renal function, mild CKD, moderate CKD and severe CKD groups are shown in Table 1. The mean age was  $57.2 \pm 11.6$  years, and there were 960 men (68%); 1089 patients (77.2%) had paroxysmal AF. Overall, radiofrequency catheter ablation and cryoballoon ablation were performed in 1336 patients (94.8%) and 74 patients (5.2%), respectively. After a mean follow-up period of  $20.7 \pm 8.8$  months, recurrence occurred in 365 patients (25.9%) overall; recurrence rates for paroxysmal and non-paroxysmal AF were 18.6% and 50.5%, respectively. Detailed baseline data, including the incidence of complications, have been reported previously [12]. There were no stroke, all-cause death or cardiac death events during the follow-up period. No patients had renal transplantation or dialysis. AF hospitalizations, need for cardioversion and repeat ablation were all events associated with early or late recurrence.



**Figure 1.** Prediction of recurrence after catheter ablation in relation to estimated glomerular filtration rate (eGFR). Area under the curve (A) = 0.74 (95% confidence interval 0.72–0.77;  $P < 0.01$ ).

**Table 3** Multivariable Cox regression analysis<sup>a</sup> of risk factors for atrial fibrillation recurrence after ablation (including estimated glomerular filtration rate with a cut-off value of 82.5 mL/min/1.73 m<sup>2</sup>).

Risk factor	HR (95% CI)	P
Age	0.99 (0.98–1.00)	0.04
AF types	1.53 (1.21–1.94)	< 0.01
Early recurrence	3.11 (2.46–3.93)	< 0.01
History of CHF	1.22 (1.00–1.48)	0.049
LAD (mm)	1.04 (1.02–1.06)	< 0.01
eGFR ≤ 82.5 (mL/min/1.73 m <sup>2</sup> )	1.79 (1.54–2.08)	< 0.01
BNP (pg/mL)	1.00 (1.00–1.01)	< 0.01
High-sensitivity CRP (mg/dL)	1.06 (1.04–1.08)	< 0.01

AF: atrial fibrillation; BNP: B-type natriuretic peptide; CHF: congestive heart failure; CI: confidence interval; CRP: C-reactive protein; eGFR: estimated glomerular filtration rate; HR: hazard ratio; LAD: left atrial diameter.

<sup>a</sup> Adjusted for sex, bundle branch block, AF duration, chronic obstructive pulmonary disease, alcohol consumption, smoking, hypertension, diabetes mellitus, stroke/transient ischaemic attack, coronary artery disease, ejection fraction, vascular disease and serum concentrations of BNP and high-sensitivity CRP.

AF recurrence rates in the normal renal function, mild CKD, moderate CKD and severe CKD groups were 11.5%, 29.3%, 72.0% and 93.3%, respectively ( $P < 0.001$ ). When comparing the four groups, mean age, left atrial size and serum concentrations of B-type natriuretic peptide (BNP) and high-sensitivity C-reactive protein (CRP) all increased with worsening renal function categories (all  $P < 0.001$ ), while the ejection fraction ( $P = 0.031$ ) and follow-up period ( $P < 0.001$ ) decreased with worsening renal function categories. As expected, the prevalence of various clinical co-morbidities increased with worsening renal function categories. Covariate regression analysis found that age, AF types, body mass index, history of congestive heart failure, left atrial diameter, eGFR and early recurrence were independent risk factors for AF recurrence (Table 2).

### Cut-off eGFR value, and predictive value for AF recurrence

Using receiver operating characteristic analysis, the area under the curve of eGFR for predicting AF recurrence was 0.74 (95% confidence interval [CI] 0.72–0.77;  $P < 0.01$ ), and the cut-off value of 82.5 mL/min/1.73 m<sup>2</sup> was derived with a specificity of 63.6% and a sensitivity of 74.5% (Fig. 1). When including this cut-off value as one of the risk factors, multivariable analysis showed that eGFR < 82.5 mL/min/1.73 m<sup>2</sup> was an independent predictor for AF recurrence (hazard ratio [HR] 1.79, 95% CI 1.54–2.08;  $P < 0.01$ ) (Table 3). Kaplan-Meier analysis shows the cumulative probability of freedom of no AF recurrence and risk of recurrence with eGFR ≥ 82.5 mL/min/1.73 m<sup>2</sup> or < 82.5 mL/min/1.73

m<sup>2</sup>, with the latter having a worse outcome (log-rank  $P < 0.01$ ) (Fig. 2).

### Renal function categories and AF recurrence

Table 4 shows the adjusted HRs for AF recurrence according to the different renal function categories defined by eGFR, with normal eGFR included as a reference group. Compared with the normal eGFR group, there was a step-wise increased risk of AF recurrence with mild CKD (HR 3.30, 95% CI 2.55–4.26;  $P < 0.01$ ), moderate CKD (HR 9.43, 95% CI 6.76–13.16;  $P < 0.01$ ) and severe CKD (HR 12.35, 95% CI 6.93–21.99;  $P < 0.01$ ) (Table 4). Patients with CKD accounted for > 72% of AF recurrences after the CA procedure. On Kaplan-Meier analysis, this trend for increased AF recurrence with worsening renal function category was significant (log-rank  $P < 0.01$ ) (Fig. 3).

### Discussion

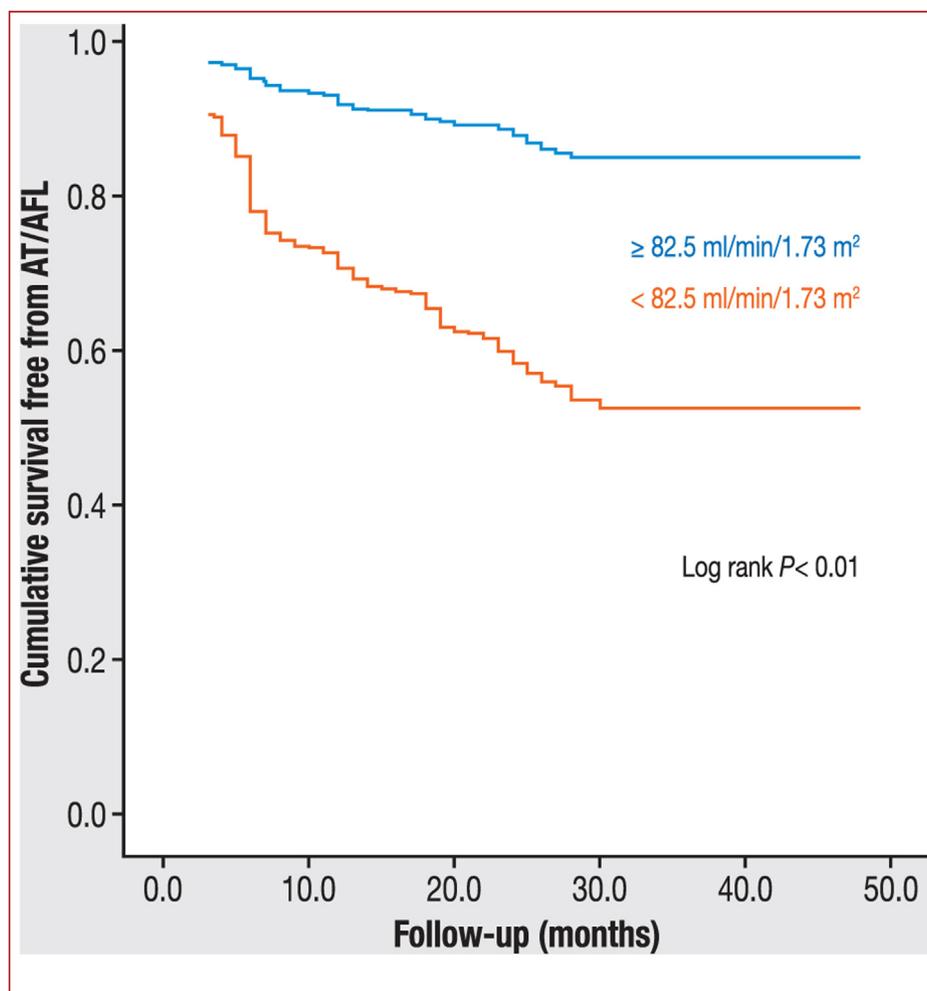
In this large cohort of Asian patients with AF, relating renal dysfunction to AF recurrence after CA, our principal findings were as follows:

- patients with worse renal function were older, had more AF recurrence after CA and clinical cardiac co-morbidities, larger left atrial size and higher concentrations of BNP and high-sensitivity CRP;
- an eGFR cut-off value of 82.5 mL/min/1.73 m<sup>2</sup> had good predictive value for AF recurrence;
- patients with mild, moderate and severe CKD had 3-, 6- and 12-fold higher risks of recurrence after CA, respectively.

To our knowledge, this is the first report on the relationship between renal function strata and AF recurrence after CA in a large Asian cohort. Our findings could help electrophysiologists to select suitable patients with AF for CA, given that low eGFR is associated with a poor outcome in terms of AF recurrence.

### The relationship between CKD and AF

CKD has been defined as an eGFR < 60 mL/min/1.73 m<sup>2</sup> over 3 months [13], and it is well known that renal dysfunction with decreased eGFR worsens cardiovascular outcomes. The incidence of AF in end-stage renal disease ranges from 10.9% to 27% and, importantly, AF increases mortality in patients with end-stage renal disease two-fold compared with in those without AF [14]. An independent graded association between reduced eGFR and the risk of cardiovascular events has been reported [3]. This is perhaps unsurprising, as AF and CKD share many risk factors and pathophysiological mechanisms. As in a previous report [6], our patients with CKD were older and had more cardiovascular co-morbidities or risk factors, such as hypertension, history of heart failure and higher serum BNP and CRP concentrations [15,16]. All of these factors may contribute to the prevalence and/or progression of both AF and CKD [17,18]. Of note, CKD also increases the risk of new onset AF, and AF increases the risk of developing kidney disease [4].



**Figure 2.** Kaplan-Meier analysis of estimated glomerular filtration rate in relation to a cut-off value of 82.5 mL/min/1.73 m<sup>2</sup>. AT: atrial tachycardia; AFL: atrial fibrillation or flutter.

CKD and AF share many pathophysiological pathways, including those related to the renin-angiotensin-aldosterone system [19–21]. Left atrial enlargement significantly increases the risk of AF recurrence after single CA [22,23], and CKD may also result in cardiac and atrial structural changes through metabolic abnormalities [24] and oxidative stress [25]. The recurrent risk after a single CA procedure in patients with AF with CKD is increased significantly (57.4% vs. 33.5% for no CKD;  $P < 0.01$ ) [6]; this is also evident in patients undergoing other energy ablations [26] or repeated radiofrequency ablations [27]. A meta-analysis by Li et al. [7] included four studies, and showed that CKD increased AF recurrence after CA (HR 1.96, 95% CI 1.35–2.85;  $P = 0.0004$ ).

Contradictory results have been reported recently. Arora et al. [28] analysed national readmission data between 2010 and 2014, and 1,128,372 patients identified as having AF by ICD-CM (International Classification of Diseases, Clinical Modification) code were included (37,360 patients underwent CA); CKD was not a significant predictor of early recurrence in patients undergoing CA in this cohort. In a study by Ullal et al. [29], in which ICD codes were also used to identify AF, CKD had no influence on late AF recurrence after CA. These two large studies included AF patients undergoing CA, but early or late arrhythmia outcomes were

only identified by ICD codes, and not by regular electrocardiogram monitoring. Despite broadly similar recurrent rates compared with our cohort, patients in those two large non-Asian cohorts [28,29] had a much higher prevalence of co-morbidities, such as hypertension, heart failure, coronary heart disease, chronic obstructive pulmonary disease and type 2 diabetes mellitus, which would weaken the influence of CKD on AF recurrence.

Some clinical predictive scores have been proposed to predict arrhythmia recurrence outcomes after CA for AF [30]; among them, the APPLE [9] and ALARMEc [31] scores include renal insufficiency as one of the risk factors, with eGFR  $< 60$  mL/min/1.73 m<sup>2</sup> and  $< 68$  mL/min/1.73 m<sup>2</sup> being used as the respective cut-off values for renal dysfunction. However, even mild decreases in eGFR may affect outcomes after CA, as shown in our study. As mentioned above, progressively severe renal dysfunction is associated with even more AF risk factors and left atrial remodelling, thereby increasing the risk of AF recurrence after CA.

### Study limitations

This study was limited by being from a single centre, and by its retrospective and observational design, but the size

**Table 4** Multivariable analysis<sup>a</sup> for atrial fibrillation recurrence according to renal function categories.

Renal function	eGFR	Adjusted HR (95% CI)	P
Normal <sup>b</sup>	≥ 90 mL/min/1.73 m <sup>2</sup>	1.000	< 0.01
Mild CKD	60–82 mL/min/1.73 m <sup>2</sup>	3.30 (2.55–4.26)	< 0.01
Moderate CKD	45–59 mL/min/1.73 m <sup>2</sup>	9.43 (6.76–13.16)	< 0.01
Severe CKD	< 45 mL/min/1.73 m <sup>2</sup>	12.35 (6.93–21.99)	< 0.01

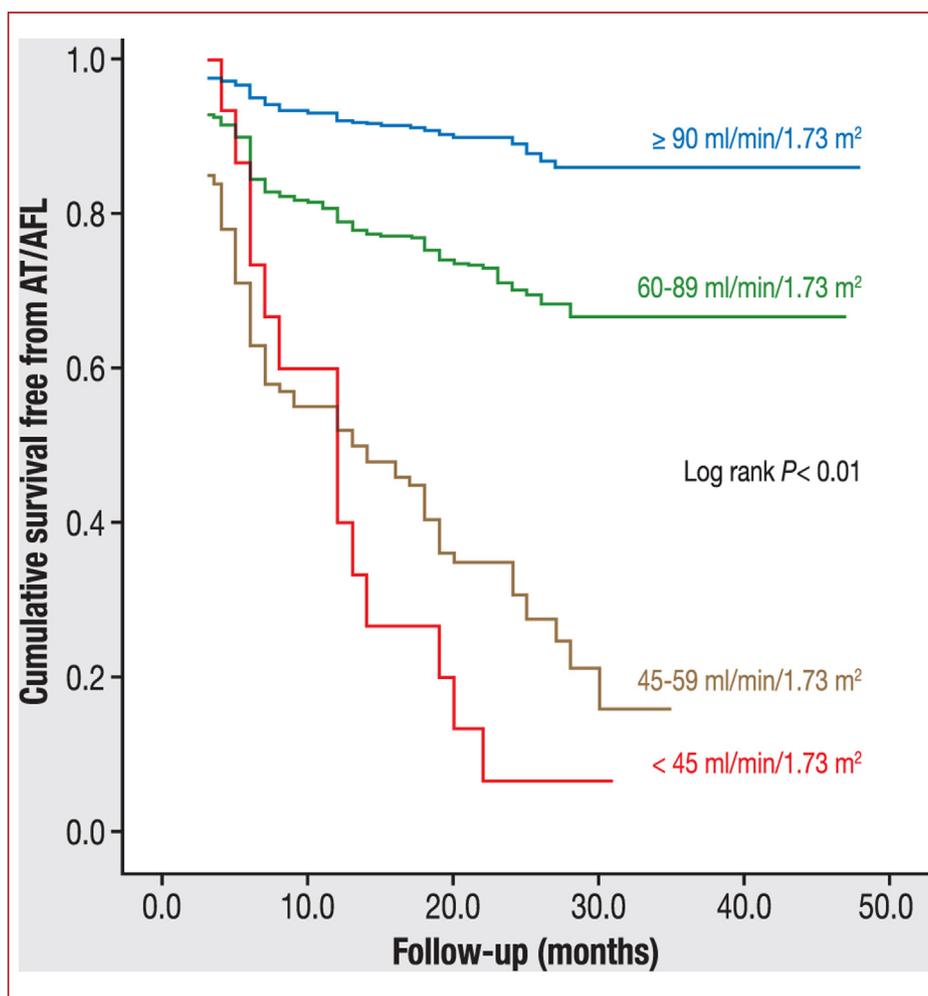
CI: confidence interval; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; HR: hazard ratio.

<sup>a</sup> Adjusted for sex, bundle branch block, AF duration, chronic obstructive pulmonary disease, alcohol consumption, smoking, hypertension, diabetes mellitus, stroke/transient ischaemic attack, coronary artery disease, ejection fraction and vascular disease.

<sup>b</sup> Reference group.

of cohort and long follow-up period are strengths. Ordinary tests such as 12-lead electrocardiograms and 24-hour Holter electrocardiograms may miss arrhythmia episodes, especially if they are asymptomatic, given their limited recording time. We also did not have complete data on the impact of

ablation per se on sequential changes in kidney function. The patients who were included for ablation were all symptomatic, and a recorded episode of symptomatic AF was required before the ablation. Symptoms were inquired about in detail at every follow-up visit.



**Figure 3.** Kaplan-Meier analysis of estimated glomerular filtration rate in relation to chronic kidney disease categories. AT: atrial tachycardia; AFL: atrial fibrillation or flutter.

## Conclusions

In a large cohort of Asian patients with AF, renal dysfunction increased the risk of AF recurrence after CA. Our findings could help decision-making regarding selection of suitable patients with AF for CA, given that low eGFR is associated with poor outcome in terms of AF recurrence.

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## Disclosure of interest

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